

Docket No. 31896-70200 (APP 98133 P1)  
Patent

### REMARKS

Claims 45, 46 and 50 are pending, and new claims 52-68 are added. By this amendment, Applicants have canceled claims 47-49 and 51 without prejudice or disclaimer. Applicants reserve the right to pursue these canceled claims in a continuation or divisional application. Applicants have amended claims 45, 46 and 50 to recite the term "S4-S5 cytoplasmic loop." This amendment is supported at least by pages 13-14 and Examples 3 and 4 of the specification.

In addition, Applicants have added claims 52-68. These claims are supported at least by page 8, line 20, to page 9, line 8; pages 12-19; page 23, line 33, to page 25, line 3; and Examples 3 and 4 of the specification.

Applicants respectfully submit that these amendments to the claims do not introduce new matter. Accordingly, Applicants respectfully request the Examiner to enter these amendments.

### Election/Restriction

On page 2, the Office Action acknowledges Applicants' election with traverse of the species Kv $\beta$ 1 and Kv1.1. The Office Action deems the restriction requirement proper and makes the requirement final. For the reasons set forth below, Applicants, once again, respectfully traverse the restriction requirement. Applicants reserve the right to petition the restriction requirement to the Commissioner under 37 C.F.R. § 1.181.

MPEP § 803.04 specifically states:

Absent evident to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 *et seq.* Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. . . . It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. (Emphasis added).

Therefore, without agreeing or disagreeing with the contention that the ion channels recited in the instant claims are distinct from each other, Applicants respectfully submit that

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the Examiner normally is required under MPEP § 803.04 to examine at least ten genes. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the restriction requirement.

**Rejection Under 35 U.S.C. § 112, First Paragraph**

On pages 2-5, the Office Action rejects claims 45-50 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled for reciting the phrase "biologically active fragment." Applicants respectfully traverse the rejection.

Applicants have canceled claims 47-49 without prejudice or disclaimer. Applicants respectfully submit that this amendment renders the rejection of these claims moot. Withdrawal of the rejection of these claims is, therefore, respectfully requested.

The Office Action contends that "Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions." However, claims 45-46 and 50 do not prescribe the positions in a protein that are tolerant to change without significantly losing the binding activity with the corresponding S4-S5 cytoplasmic loop or amino-terminal inactivation region. Instead, claims 45-46 and 50, as presented herein, encompass the use of any fragment that retains the binding activity with the corresponding S4-S5 cytoplasmic loop or amino-terminal inactivation region. Claims 45-46 and 50 contemplate any modification (e.g., substitution, deletion, insertion, or posttranslational modification) that can be introduced into a parent sequence. A polypeptide thus modified can be tested for its binding activity with the corresponding S4-S5 cytoplasmic loop or amino-terminal inactivation region. The methods for carrying out this test are set forth in detail in Example 3 and other parts of the specification. It is, therefore, readily apparent that the determination of whether a given polypeptide variant can or cannot bind to an S4-S5 cytoplasmic loop or an amino-terminal inactivation region does not involve any unpredictable arts, does not entail extensive screening, and therefore, does not require undue experimentation. If, however, the Examiner does not agree, Applicants respectfully request that the Examiner present a specific polypeptide whose binding activity with an S4-S5 cytoplasmic loop or amino-terminal inactivation region cannot be readily assessed according to the present application.

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Based on the above reasons, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of lack of enablement and that one of ordinary skill in the art can readily make and use a biologically active fragment of an S4-S5 cytoplasmic loop or an amino-terminal inactivation region by simply testing whether the fragment can bind to the corresponding amino-terminal inactivation region or S4-S5 loop. No positional information is required for such testing. Accordingly, reconsideration and withdrawal of the nonenablement rejection are respectfully requested.

On pages 6-7, the Office Action also rejects claims 45-50 under 35 U.S.C. §112, first paragraph, as allegedly not satisfying the written description requirement. Applicants respectfully traverse this rejection also.

As noted, Applicants have herein canceled claims 47-49 without prejudice or disclaimer, and Applicants respectfully submit that this amendment renders the rejection of these claims moot. Reconsideration and withdrawal of the written description rejection of claims 45, 46, and 50 are, therefore, respectfully requested.

The Office Action argues that the "specification and claim[s] do not indicate what distinguishing attributes shared by the members of the genus" and that "[s]tructural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure." Applicants respectfully point out, however, that claims 45-46 and 50 do not claim structural features that can distinguish compounds in a genus. Claims 45-46 and 50 are directed to the use of a biologically-active fragment of an S4-S5 loop or an amino-terminal inactivation region. Such a fragment can be readily determined based on the reasons set forth above. If, however, the Examiner does not agree, Applicants respectfully request that the Examiner present a specific variant, of which one of ordinary skill in the art would believe that Applicants had not had possession at the time the present application was filed.

Based on the foregoing, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of lack of written description and that at least claims 45-46 and 50 meet the written description requirement. Reconsideration and withdrawal of these rejections are, therefore, respectfully requested.

**Rejection Under 35 U.S.C. § 102**

On page 7, the Office Action rejects claims 45-46 as being anticipated by the Stephens et al. article (1996) (hereinafter "Stephens"). Applicants respectfully traverse the rejection.

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In view of the amendments to the claims herein, Applicants respectfully submit that Stephens fails to teach or suggest modulation of the interactions between an S4-S5 cytoplasmic loop and an amino-terminal inactivation region. In addition, Stephens does not teach testing a compound other than an ion channel or an amino-terminal inactivation region thereof for the inhibitory effect on the binding between an S4-S5 loop and an amino-terminal inactivation region. Therefore, Stephens fails to teach each and every element of claims 45 and 46. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the § 102(b) rejection.

**Rejection Under 35 U.S.C. § 103**

On pages 8-10, the Office Action rejects claims 47-50 as being obvious over the Wang et al. article (1996) (hereinafter "Wang") in view of U.S. Patent No. 6,080,557 to Sims et al. (hereinafter "Sims"). Applicants respectfully traverse this rejection also.

As noted, Applicants have canceled claims 47-49 without prejudice or disclaimer, thereby rendering the rejection of these claims moot. Withdrawal of the rejection of claims 47-49, is therefore, respectfully requested.

Applicants also submit that Wang and Sims, individually or in combination, fail to teach or suggest modulation of the interactions between an S4-S5 cytoplasmic loop and an amino-terminal inactivation domain, as set forth in the claimed invention, and thus fail to teach or suggest all of the elements in claim 50. See MPEP § 2143.03 ("To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art").

In fact, Wang teaches away from claim 50. On page 28313, right column, Wang states that "the binding site is within the 159 amino acids immediately preceding the putative S1 transmembrane domain." Wang does not suggest any interaction between an S4-S5 loop and an amino-terminal inactivation region. Sims is generally directed towards signal transduction pathways associated with inflammation, and adds little if anything, to Wang, and, therefore, does not remedy the deficiencies of Wang.

Moreover, the Office Action has failed to establish any motivation to combine. The Federal Circuit has repeatedly emphasized that evidence of a motivation to combine must accompany a challenge based on multiple references. See *In re Dembiczak*, 175 F.3d 994 (Fed. Cir. 1999) and *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534 (Fed. Cir. 1998). See also MPEP §2143.01 (The prior art must suggest the desirability of the claimed invention). A

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statement that combination of the prior art to meet the claimed invention would have been within the ordinary skill in the art is not alone sufficient to establish a *prima facie* case of obviousness. See MPEP §2143.01.

Based on all of the above reasons, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of obviousness. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claim 50.

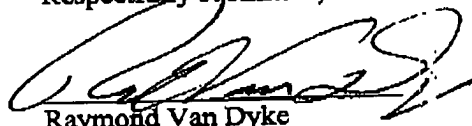
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### CONCLUSION

For at least the reasons set forth above, Applicants respectfully submit that this application is in condition for allowance. Favorable consideration and prompt allowance of the claims are earnestly solicited. Although Applicants believe that no fee is due, the Commissioner is hereby authorized to charge any payment deficiency to deposit account number 19-2380 referring to attorney docket number 031896-070200.

Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,



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